```
=> d que stat l11
L1             1 SEA FILE=REGISTRY ABB=ON  "HPTH-(1-34)"/CN
L2             1 SEA FILE=REGISTRY ABB=ON  "VITAMIN D"/CN
L3             1 SEA FILE=REGISTRY ABB=ON  CALCIUM/CN
L4        161514 SEA FILE=HCAPLUS ABB=ON  (?BONE?(3A)(?FRACT? OR ?FORM? OR
                 ?LOSS? OR ?LOSE?) OR ?OSTEPOROSIS? OR ?OSTEOGENESIS? OR
                 ?SPINE? OR ?SPINAL?)
L5          1004 SEA FILE=HCAPLUS ABB=ON  L4 AND (L1 OR HPTH(W)(1-34) OR ?HPTH?
                 OR ?HUMAN?(W)?PARATHYROID?(W)?HORMONE?(3W)(1-34) OR ?HORMONE?(W
                 )?REPLACEMENT?(W)?THERAPY?)
L6           300 SEA FILE=HCAPLUS ABB=ON  L5 AND (L2 OR L3 OR ?VITAMIN?(W)D OR
                 CA OR ?CALCIUM?)
L7           229 SEA FILE=HCAPLUS ABB=ON  L6 AND (AGE? OR ?AGING? OR ?GERIAT?
                 OR ?SENIL? OR ?MENOPAUS? OR ?KLINEFELTER?(W)?SYNDROM? OR
                 ?HYPOGONAD? OR ?GONAD?(W)?DISORDER?)
L8           168 SEA FILE=HCAPLUS ABB=ON  L7 AND (?HUMAN? OR ?PATIENT?)
L9             2 SEA FILE=HCAPLUS ABB=ON  L8 AND (?REDUCE? OR ?LESSEN? OR
                 ?CONTROL? OR ?DECREAS?)(W)?RISK?
L10          168 SEA FILE=HCAPLUS ABB=ON  L8 OR L9
L11           28 SEA FILE=HCAPLUS ABB=ON  L10 AND (?METHOD? OR ?TECHNIQ?)
=> d ibib abs l11 1-28

L11  ANSWER 1 OF 28  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:857916  HCAPLUS
TITLE:                    Soymilk or progesterone for prevention of bone
                          loss: A 2 year randomized, placebo-controlled
                          trial
AUTHOR(S):                Lydeking-Olsen, Eva; Beck-Jensen, Jens-Erik; Setchell,
                          Kenneth D. R.; Holm-Jensen, Trine
CORPORATE SOURCE:         Institute for Optimum Nutrition, Copenhagen, 1452,
                          Den.
SOURCE:                   European Journal of Nutrition (2004), 43(4), 246-257
                          CODEN: EJNUFZ; ISSN: 1436-6207
PUBLISHER:                Steinkopff Verlag
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Background Given concerns over the use of hormone
     replacement therapy (HRT), women are seeking natural
     alternatives to cope with the symptoms and effects of menopause.
     The bone sparing effects of soy protein and its isoflavones is well
     established in animal studies, while 5 previous human studies on
     soy and bone have yielded variable outcomes due in part to their short
     duration of study.  Progesterone has been suggested as a bone-trophic
     hormone, but the effect of long-term, low dose transdermal progesterone is
     unknown.  Aim The aim of the study was to compare for the first time the
     long-term effects of soymilk, with or without isoflavones with natural
     transdermal progesterone, or the combination, on bone mineral d. in the
     lumbar spine and hip.  Methods Postmenopausal
     , Caucasian women with established osteoporosis or at least 3 risk-factors
     for osteoporosis, were randomly assigned, double-blind to one of four
     treatment-groups: soymilk containing isoflavones (soy+, n=23), transdermal
     progesterone (TPD+, n=22), or the combination of soy+ and TDP+, (n=22) or
     placebo (isoflavone-poor soymilk, soy÷ and progesterone-free-cream
     TDP÷, n=22).  All subjects received comparable intakes of
     calcium, minerals and vitamins.  Bone mineral content (BMC) and d.
     (BMD) were measured in lumbar spine and hip by using dual-energy
     X-ray absorptiometry (DEXA) at baseline and after 2 yr.  Findings The
     percentage change in lumbar spine BMD and BMC resp., did not
     differ from zero in the soy+ group (+1.1%, +2.0%) and TDP+ group
     (÷1.1%, +0.4%) but significant bone loss occurred
```

in the control group (÷4.2%, ÷4.3%) and the combined treatment group (÷2.8%, ÷2.4%). No significant changes occurred for femoral neck BMD or BMC. Interpretation Daily intake of two glasses of soymilk containing 76 mg isoflavones prevents lumbar **spine bone loss** in **postmenopausal** women. Transdermal progesterone had bone-sparing effects but when combined with soy milk a neg. interaction between the two treatments occurs resulting in **bone-loss** to a greater extent than either treatment alone.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:640109 HCAPLUS
DOCUMENT NUMBER: 141:253360
TITLE: Teriparatide: a review
AUTHOR(S): Quattrocchi, Elaena; Kourlas, Helen
CORPORATE SOURCE: Pharmacy Practice Department, Arnold and Marie Schwartz College of Pharmacy and Health Sciences, Long Island University, Brooklyn, NY, USA
SOURCE: Clinical Therapeutics (2004), 26(6), 841-854
CODEN: CLTHDG; ISSN: 0149-2918
PUBLISHER: Excerpta Medica, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Background: Traditionally, the management of osteoporosis in men and women has included the use of antiresorptive **agents** in combination with **calcium** and **vitamin D** supplementation. The mechanism of action of teriparatide is unique in that it possesses anabolic properties and therefore builds bone. Since the approval of teriparatide in the United States in 2002, a great deal of interest regarding its use in osteoporosis has developed. Objectives: This article reviews the information available on the new recombinant **human parathyroid hormone** teriparatide (**hPTH [1-34]**), including its clin. pharmacol., mechanism of action, pharmacokinetic properties, clin. efficacy, safety profile, potential drug interactions, contraindications and warnings, dosage and administration, and pharmacoeconomics. **Methods**: The articles included in this review were identified through searches of PubMed and MEDLINE (1966-Dec. 2003) and International Pharmaceutical Abstrs. (1970-Dec. 2003). Search terms included teriparatide, Forteo, recombinant **human parathyroid hormone** (**1-34**), and osteoporosis. The refs. of the identified articles were reviewed for addnl. publications. Specific product information was also obtained from the manufacturer of teriparatide. Results: Teriparatide has been studied in **postmenopausal** women with osteoporosis, drug-induced osteoporosis (specifically, corticosteroid-induced osteoporosis), and men with osteoporosis. The data available from various clin. trials have shown an increase in both bone mineral d. (BMD) and bone mineral content (BMC) with the use of teriparatide compared with placebo. One study found that women treated with the 20-μg dose and the 40-μg dose were 35% and 40%, resp., less likely to have one or more new nonvertebral fractures compared with placebo ($P = 0.02$). Another study compared the use of daily teriparatide 40-μg injections vs. oral daily alendronate. Results showed that the incidence of nonvertebral fractures was significantly lower in the teriparatide group than the alendronate group ($P < 0.05$). A study using 20- and 40-μg daily injections of teriparatide was performed in men with osteoporosis. There was a statistically significant increase in lumbar **spine** BMD of 5.9% in the 20-μg group and 9.0% in the 40-μg group (both, $P < 0.001$). In the femoral neck, a 1.5% increase in

BMD occurred in the 20-μg group (P = 0.021) and a 0.9% increase in the 40-μg group (P < 0.001). A limited number of studies are available assessing the combination of antiresorptive medications and teriparatide; however, the available data suggest that the effects of teriparatide do not require prior stimulation of bone resorption. Conclusions: Teriparatide has been shown clin. to improve BMD and BMC in **postmenopausal** women and in men. Because of its anabolic capabilities, teriparatide can be used as an alternative to the traditional therapies that are currently available for the treatment of osteoporosis, with scheduled monitoring for adverse effects such as hypercalcemia and urinary **calcium** excretion. In 1 study, mild hypercalcemia was seen most often 4 to 6 h after SC injection of teriparatide before returning to normal. Urinary, **calcium** was observed to increase by 30 mg/d (0.75 mmol/d) with teriparatide.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:453015 HCAPLUS
DOCUMENT NUMBER: 141:17632
TITLE: **Methods** and **agents** elevating cAMP and **calcium** ion for increasing neurogenesis
INVENTOR(S): Bertilsson, Goran; Erlandsson, Rikard; Frisen, Jonas; Haegestrand, Anders; Heidrich, Jessica; Hellstrom, Kristina; Haggblad, Johan; Jansson, Katarina; Kortesmaa, Jarkko; Lindquist, Per; Lundh, Hanna; McGuire, Jacqueline; Mercer, Alex; Njberg, Karl; Ossoinak, Amina; Patrone, Cesare; Ronnholm, Harriet; Zachrisson, Olof; Wikstrom, Lilian
PATENT ASSIGNEE(S): Neuronova AB, Swed.
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004045592	A2	20040603	WO 2003-IB5311	20031120
WO 2004045592	A3	20041104		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-427912P P 20021120

AB The invention discloses **methods** for promoting neurogenesis by contacting neuronal tissue with intracellular cAMP-elevating **agents** and intracellular **calcium** ion-elevating **agents**. **Agents** for promoting neurogenesis are also disclosed.

L11 ANSWER 4 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:414626 HCAPLUS
DOCUMENT NUMBER: 140:417976
TITLE: **Method** of treating osteoporosis and other bone disorders with upfront loading of bisphosphonates, and kits for such treatment
INVENTOR(S): Wimalawansa, Sunil J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 23 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

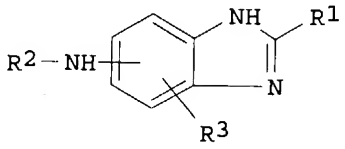
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004097468	A1	20040520	US 2002-299975	20021120
PRIORITY APPLN. INFO.:			US 2002-299975	20021120

AB Administering thereto-upfront loading of a bisphosphonate **agent** can be used to treat primary and secondary osteoporosis, other metabolic bone diseases, alleviation of bone pain, transplant and drug-induced **bone loss**, Paget's disease of bone, loosening of prosthesis, or metastatic bone diseases in mammals, preferably a **human** female or a male. A bisphosphonate drug can be administered as a loading dose upfront. Bisphosphonates can be administered by themselves or combined with, one or more other medications acting on bone, such as HRT, selective estrogen receptor modulating drug, calcitonin, parathyroid hormone, fluoride, androgen, sex-steroid hormone analogs, nitroglycerin growth factors and their analogs, peptides and proteins and their analogs, or any other novel therapeutic **agents.** This new regimen of administration of an anti-osteoporosis drug (e.g., a bisphosphonate) by itself, or in combination with other medications, can be used in mammals, preferably **human** (in women and men) for prevention and treatment of osteoporosis (e.g., **postmenopausal**, glucocorticoid- or drug-induced osteoporosis and osteoporosis in men, etc.) and other metabolic bone disorders, metastatic bone disease, transplant bone disease, Paget's disease, and prevention and treatment of loosening of prosthesis. Disclosed are **methods** for rapid inhibition of bone resorption in mammals while obtaining a rapid reduction of bone turnover and biomarkers, rapid increase of bone mineral d., and rapid reduction of fractures. Also disclosed are pharmaceutical compns. and kits for carrying out the therapeutic **methods** disclosed herein.

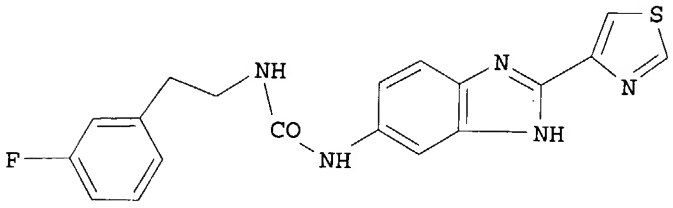
L11 ANSWER 5 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:412812 HCAPLUS
DOCUMENT NUMBER: 140:406808
TITLE: Preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators
INVENTOR(S): Kim, Yuntae; Spencer, Keith L.; Hanney, Barbara; Duggan, Mark E.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 136 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2004041277 A1 20040521 WO 2003-US34345 20031028
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2002-422914P P 20021101
OTHER SOURCE(S): MARPAT 140:406808
GI



I



II

AB Carbonylamino-benzimidazoles (shown as I; variables defined below; e.g. II) are modulators of the androgen receptor (AR) in a tissue selective manner. They are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male **patient** or in the uterus of a female **patient.** These compds. are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, **bone fracture**, **bone** damage following **bone** reconstructive surgery, sarcopenia, frailty, **aging** skin, male **hypogonadism**, **postmenopausal** symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, arthritic condition and joint repair, HIV-wasting, prostate cancer, cancer cachexia, Alzheimer's disease, muscular dystrophies, premature ovarian failure, and autoimmune disease, alone or in combination with other active **agents.** Although the **methods** of preparation are not claimed, 6 example prepns. and characterization data for .apprx.150 examples of I are included; nearly all examples contain the thiazol-4-yl group at the 2 position of the benzimidazole. For example, II was prepared from 3-fluorophenethylamine, 1,1'-carbonyldiimidazole and [2-(thiazol-4-yl)-3H-benzimidazol-5-yl]amine, the latter of which was prepared from thiazole-4-carboxylic acid and (4-amino-3-nitrophenyl)carbamic acid tert-Bu ester (preparation described) via amide formation followed by cyclization in 20% aqueous AcOH. For I: R1 = aryl or heterocyclyl; R2 =

-(C:O)NR5R6, -(C:O)a(C1-10)alkyl, -(C:O)a(C2-8)alkenyl, -(C:O)a(C2-8)alkynyl, -(C:O)a(C3-10)cycloalkyl, -(C:O)a(C3-8)heterocyclyl, and -(C:O)aaryl; R3 = H, halogen, -(C:O)aOb(C1-10)alkyl, -(C:O)aOb(C2-8)alkenyl, -(C:O)aOb(C2-8)alkynyl, -(C:O)aOb(C3-10)cycloalkyl, -(C:O)aOb(C3-8)heterocyclyl, -(C:O)aObaryl, -(C:O)aNR5R6, -Ob(C:O)NR5R6, -NR5(C:O)aObRb, -NR5(C:O)NR5R6, -NR5S(O)2Rb, -(C:O)OH, trifluoromethoxy, trifluoroethoxy, -Ob(C1-10)perfluoroalkyl, -S(O)2Ob(C1-10)alkyl, -S(O)2Ob(C2-8)alkenyl, -S(O)2Ob(C2-8)alkynyl, -S(O)2Ob(C3-10)cycloalkyl, -S(O)2Ob(C3-8)heterocyclyl, -S(O)2Obaryl, -NR5S(O)2NR5R6, -CN, -NO2, oxo, and -OH; a = 0-1; b = 0-1; addnl. details are given in the claims.

L11 ANSWER 6 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:325938 HCAPLUS
DOCUMENT NUMBER: 141:325890
TITLE: Transdermal **hormone replacement therapy** improves vertebral bone density in primary biliary cirrhosis: results of a 1-year controlled trial
AUTHOR(S): Pereira, S. P.; O'Donohue, J.; Moniz, C.; Phillips, M. G.; Abraha, H.; Buxton-Thomas, M.; Williams, R.
CORPORATE SOURCE: Institute of Liver Studies, King's College Hospital, London, UK
SOURCE: Alimentary Pharmacology and Therapeutics (2004), 19(5), 563-570
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Retrospective studies have suggested that **hormone replacement therapy** may reduce the rate of **bone loss** in primary biliary cirrhosis, but no controlled data are available. **Methods**: Forty-two post-**menopausal** women with primary biliary cirrhosis were treated with **calcium** and **vitamin D**, either alone (n = 21) or together with transdermal **hormone replacement therapy** (n = 21). **Bone** densitometry was **performed** at baseline and at 1 yr, and serum and urinary markers of bone turnover were measured at three-monthly intervals. Results: At entry, 17 **patients** (40%) had **spinal** or femoral osteopenia (T score -1 to -2.5) and nine (21%) had osteoporosis (T < -2.5). In those given **hormone replacement therapy**, there was a significant decrease in the mean urinary deoxypyridinoline:creatinine ratios at 3 mo (7.8 vs. 6.1 nM/mM creatinine for no **hormone replacement therapy** vs. **hormone replacement therapy**; P = 0.04) and a 48% reduction in urinary **calcium** excretion at 1 yr (0.66 vs. 0.32 nM/mM creatinine; P = 0.01). Repeat bone densitometry at 1 yr revealed a 2.25% increase in the **hormone replacement therapy** group (P = 0.02), compared with a non-significant 0.87% decrease in L2-L4 bone mineral d. in those not given **hormone replacement therapy**. Both treatment regimens were well tolerated, with no increase in cholestasis. Conclusions: Compared with **calcium** and **vitamin D** alone, supplemental treatment with transdermal **hormone replacement therapy** for 1 yr improved the vertebral bone d. and urinary markers of bone turnover in post-**menopausal** women with primary biliary cirrhosis.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:1009405 HCAPLUS
DOCUMENT NUMBER: 140:140040
TITLE: Both **hPTH(1-34)** and bFGF increase trabecular bone mass in osteopenic rats but they have different effects on trabecular bone architecture
AUTHOR(S): Lane, Nancy E.; Yao, Wei; Kinney, John H.; Modin, Gunnard; Balooch, Mehdi; Wronski, Thomas J.
CORPORATE SOURCE: Department of Medicine, University of California at San Francisco, San Francisco, CA, USA
SOURCE: Journal of Bone and Mineral Research (2003), 18(12), 2105-2115
CODEN: JBMREJ; ISSN: 0884-0431
PUBLISHER: American Society for Bone and Mineral Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Materials and **Methods**: Six-month-old female Sprague-Dawley rats (n = 74) were ovariectomized (OVX) or sham-operated (sham) and maintained untreated for 2 mo. Then OVX rats were s.c. injected with basic fibroblast factor (bFGF; 1 mg/kg, 5 days/wk), **human parathyroid hormone** [**hPTH(1-34)**; 40 μg/kg, 5 days/wk], or vehicle for 60 days (days 60-120). Sham-operated and one group of OVX animals were injected with vehicle. Biochem. markers of bone turnover (urinary deoxypyridinoline cross-links; Quidel Corp., San Diego, **CA**, USA) and serum osteocalcin (Biomedical Technologies, Stroughton, MA, USA) were obtained at study days 0, 60, 90, and 120 and analyzed by ELISA. At death, the right proximal tibial metaphysis was removed, and microcomputed tomog. was **performed** for trabecular **bone** structure and processed for histomorphometry to assess bone cell activity. The left proximal tibia was used for nanoindentation/mech. testing of individual trabeculae. The data were analyzed with Kruskal Wallis and post hoc testing as needed. Results: Ovariectomy at day 60 resulted in about a 50% **loss** of trabecular **bone** volume compared with sham-treated animals. By day 120 post-OVX, OVX + vehicle treated animals had decreased trabecular bone volume, connectivity, number, and high bone turnover compared with sham-operated animals [$p < 0.05$ from sham-, **hPTH(1-34)**-, and bFGF-treated groups]. Treatment of OVX animals with bFGF and **hPTH(1-34)** both increased trabecular bone mass, but **hPTH(1-34)** increased trabecular thickness and bFGF increased trabecular number and connectivity. Histomorphometry revealed increased mineralizing surface and **bone formation** rate in both bFGF and **hPTH(1-34)** animals. However, osteoid volume was greater in bFGF-treated animals compared with both the **hPTH(1-34)** and OVX + vehicle animals ($p < 0.05$). Nanoindentation by atomic force microscope was performed on approx. 20 individual trabeculae per animal (three animals per group) and demonstrated that elastic modulus and hardness of the trabeculae in bFGF-treated animals were similar to that of the **hPTH**-treated and sham + vehicle-treated animals. Conclusion: Both **hPTH(1-34)** and bFGF are anabolic **agents** in the osteopenic female rat. However, **hPTH(1-34)** increases trabecular bone volume primarily by thickening existing trabeculae, whereas bFGF adds trabecular bone mass through increasing trabecular number and trabecular connectivity. These results suggest the possibility of sequential treatment paradigms for severe osteoporosis.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:1006711 HCAPLUS
DOCUMENT NUMBER: 140:53961
TITLE: Analogs of parathyroid hormone and PTH-related protein as bone anabolic **agents**
INVENTOR(S): Chorev, Michael; Rosenblatt, Michael
PATENT ASSIGNEE(S): Beth Israel Deaconess Medical Center, Inc., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003105772	A2	20031224	WO 2003-US18890	20030613
WO 2003105772	A3	20040408		

W: AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-388918P P 20020613
US 2002-398005P P 20020723

OTHER SOURCE(S): MARPAT 140:53961
AB The invention provides novel parathyroid hormone analogs and parathyroid hormones-related protein analogs. The invention also provides **methods** of using these analogs to treat osteoporosis, promote the **formation** of **bone**, and inhibit **bone loss**. The **method** of the invention can further comprise administering an addnl. pharmaceutical **agent** which is a bone resorption inhibitor or **bone formation** promoter. Pharmaceutical prepns. containing the compds. of the invention are further claimed.

L11 ANSWER 9 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:765982 HCAPLUS
DOCUMENT NUMBER: 139:316954
TITLE: Evaluation of bone mineral density after renal transplantation under a tacrolimus-based immunosuppression: a pilot study
AUTHOR(S): Goffin, E.; Devogelaer, J.-P.; Depresseux, G.; Squifflet, J.-P.; Pirson, Y.; van Ypersele de Strihou, C.
CORPORATE SOURCE: Department of Nephrology, Hopital St. Luc, Universite Catholique de Louvain, Brussels, Belg.
SOURCE: Clinical Nephrology (2003), 59(3), 190-195
CODEN: CLNHBI; ISSN: 0301-0430
PUBLISHER: Dustri-Verlag Dr. Karl Feistle
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: Progressive **bone loss** consistently complicates renal transplantation (TP) in **patients** given an

immunosuppression including prednisolone. The adjunction of cyclosporine in the immunosuppressive regimen does not reverse the neg. impact of renal TP on the skeleton. The post-transplant effect of tacrolimus on bone mass is still unknown. **Methods**: We evaluated the evolution of bone mineral d. (BMD) and various biochem. markers over the first 12 mo following renal TP in 23 **patients** given an immunosuppression combining tacrolimus and low-dose prednisolone. BMD of lumbar **spine**, total hip and hip subregions was measured by dual-energy x-ray absorptiometry within the first 15 days and 1 yr after TP. Results: At the time of TP, the average BMD was low in both the lumbar **spine** and the hip. After TP, a normalization of serum creatinine and a decrease in serum phosphate and iPTH levels occurs. Serum alkaline phosphatase level significantly rose transiently within the first 6 mo and decreased thereafter. At 1 yr post TP, BMD remained unchanged in the lumbar and in the trochanter subregions and rose in the other sites. BMD increased by at least 2% in 8, 13, 10 and 10 out of the 23 **patients** in the lumbar, neck, trochanter and total hip subregions, resp. No correlation was found between evolution in BMD and **age**, sex, dialysis duration, level of hyperparathyroidism, prednisolone and tacrolimus cumulative intake and prescription of **calcium**, **vitamin D** or **hormone replacement therapy.** Conclusions: An immunosuppression combining tacrolimus and low-dose prednisolone might avoid the usual post-TP **bone loss.** Further randomized double-blind studies evaluating a larger cohort of **patients** should be undertaken to compare the effect of cyclosporine and tacrolimus on bone mass.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:477224 HCAPLUS
DOCUMENT NUMBER: 139:207969
TITLE: Effect of **hormone replacement therapy** on bone quality in early **postmenopausal** women
AUTHOR(S): Paschalis, E. P.; Boskey, A. L.; Kassem, M.; Eriksen, E. F.
CORPORATE SOURCE: Mineralized Tissues Research Section, Hospital for Special Surgery, New York, NY, USA
SOURCE: Journal of Bone and Mineral Research (2003), 18(6), 955-959
CODEN: JBMREJ; ISSN: 0884-0431
PUBLISHER: American Society for Bone and Mineral Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB HRT is an effective prophylaxis against **postmenopausal bone loss.** IR **imaging** of paired iliac crest biopsies obtained at baseline and after 2 yr of HRT therapy demonstrate an effect on the mineral crystallinity and collagen crosslinks that may affect bone quality. Several studies have demonstrated that hormonal replacement therapy (HRT) is an effective prophylaxis against **postmenopausal bone loss**, although the underlying mechanisms are still debated. IR spectroscopy has been used previously for analyzing bone mineral crystallinity and three-dimensional structures of collagen and other proteins. In the present study, the **technique** of Fourier transform IR microscopic **imaging** (FTIRI) was used to investigate the effect of estrogen on bone quality (arbitrarily defined as mineral/matrix ratio, mineral crystallinity/maturity, and relative ratio of collagen crosslinks [pyridinoline/deH-DHLNL]) at the ultrastructural level, in mineralized,

thin tissue sections from double (before and after administration of HRT regimen; cyclic estrogen and progestogen [norethisterone acetate]) iliac crest biopsy specimens from 10 healthy, early **postmenopausal** women who were not on any medication with known influence on **calcium** metabolism FTIRI allows the anal. of undemineralized thin tissue sections (each image analyzes a 400 + 400 μM2 area with a spatial resolution of .apprx.6.3 mm). For each bone quality variable considered, the after-treatment data exhibited an increase in the mean value, signifying definite changes in bone properties at the mol. level after HRT treatment. Furthermore, these findings are consistent with suppressed osteoclastic activity.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:355828 HCAPLUS
DOCUMENT NUMBER: 138:363217
TITLE: Uses of parathyroid hormone antagonists for the diagnosis and treatment of diseases associated with **bone** mineral **loss**
INVENTOR(S): Cantor, Thomas L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U.S. Ser. No. 928,047.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003087822	A1	20030508	US 2002-215770		20020809
US 2002160945	A1	20021031	US 2001-928047		20010810
PRIORITY APPLN. INFO.:			US 1999-323606	B2	19990602
			US 2000-224446P	P	20000810
			US 2000-224447P	P	20000810
			US 2000-636530	A2	20000810
			US 2001-928047	A2	20010810

AB The present invention relates to parathyroid hormone (PTH) antagonists. More particularly, the present invention provides for pharmaceutical compns., kits and combinations comprising the PTH antagonist. The present invention also provides for **methods** for preventing, treating or delaying a disease or disorder associated with excessive bone mineral, e.g., **calcium**, loss or for preventing, treating or delaying the effect of a PTH agonist using the PTH antagonist. The present invention further provides for **methods** for identifying a subject having or at risk of having osteoporosis or decreased bone d., or for identifying a subject in need of PTH antagonist treatment, or for monitoring a subject undergoing treatment for osteoporosis or decreased bone d., by determining and/or monitoring PTH antagonist level or a comparative value between PTH agonist and PTH antagonist. The present invention further provides for **methods** for identifying an **agent** suitable for preventing, treating or delaying osteoporosis by identifying a compound that enhances the PTH antagonist activity.

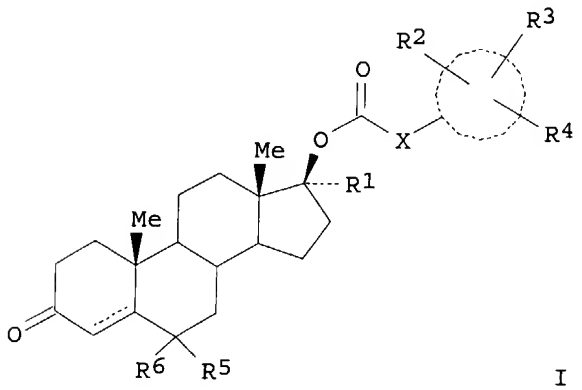
L11 ANSWER 12 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:261603 HCAPLUS
DOCUMENT NUMBER: 138:281598
TITLE: Androstane compounds as androgen receptor (AR)

modulators for the treatment of AR-related diseases
INVENTOR(S): Wang, Jiabing
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003026568	A2	20030403	WO 2002-US29436	20020917
WO 2003026568	A3	20040226		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1429779	A2	20040623	EP 2002-766288	20020917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2004235808	A1	20041125	US 2004-489072	20040308
PRIORITY APPLN. INFO.:			US 2001-324124P P	20010921
			WO 2002-US29436 W	20020917

OTHER SOURCE(S): MARPAT 138:281598
GI



I

AB Compds. of structural formula (I) as herein defined are claimed as useful in a **method** for modulating a function of the androgen receptor in a tissue selective manner in a **patient** in need of such modulation, as well as in a **method** of activating the function of the androgen receptor in a **patient**, and in particular the **method** wherein the function of the androgen receptor is blocked in the prostate of a male **patient** or in the uterus of a female **patient** and activated in bone and/or muscle tissue. These compds. are useful in the treatment of conditions caused by androgen deficiency or

which can be ameliorated by androgen administration, including osteopenia, osteoporosis, periodontal disease, **bone fracture**, **bone** damage following **bone** reconstructive surgery, sarcopenia, frailty, **aging** skin, male **hypogonadism**, female sexual dysfunction, **postmenopausal** symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, aplastic anemia and other hematopoietic disorders, pancreatic cancer, renal cancer, prostate cancer, inflammatory arthritis and joint repair, alone or in combination with other active **agents. Methods** for the co-administration of those compds. with bone-strengthening **agents** are also claimed.

L11 ANSWER 13 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:136354 HCAPLUS
DOCUMENT NUMBER: 139:224064
TITLE: Teriparatide has no effect on the **calcium** -mediated pharmacodynamics of digoxin
AUTHOR(S): Benson, Charles T.; Voelker, James R.
CORPORATE SOURCE: Lilly Laboratories for Clinical Research, Indianapolis, IN, USA
SOURCE: Clinical Pharmacology & Therapeutics (St. Louis, MO, United States) (2003), 73(1), 87-94
CODEN: CLPTAT; ISSN: 0009-9236
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: Teriparatide (recombinant **human parathyroid hormone** [**1-34**]) stimulates **bone formation** and causes small transient increases in serum **calcium** concentration We assessed whether teriparatide causes a change in digoxin pharmacodynamic effects by measuring systolic time intervals and heart rate. **Methods**: Measurements were made by echocardiog. Doppler that examined 3 systolic time intervals, as follows: QS2 (time from Q wave on ECG to the closure of the aortic valve), left ventricular ejection time, and pre-ejection period, all corrected for changes in heart rate. Fifteen healthy subjects (2 men and 13 women) were administered a single s.c. teriparatide dose (20 μg) on day 1 and then equilibrated on a daily oral dose of digoxin for 15 days. S.C. placebo and teriparatide, 20 μg, were given in a randomized crossover design with the 14th (day 15) and 15th (day 16) digoxin doses. Serial systolic time interval and heart rate measurements were obtained on days 1, 15, and 16. Results: After subjects were dosed to steady state with digoxin, there were statistically significant redns. in QS2 corrected for heart rate (QS2c) of 23 to 25 ms and heart rate of 4 to 6 beats/min. However, there was no difference between treatment with digoxin plus placebo vs. digoxin plus teriparatide. The study was powered to find a difference in QS2c as small as 6 ms (α =.05, β =.2). Conclusion: Teriparatide, 20 μg s.c., does not alter the cardiac effect of digoxin.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:108584 HCAPLUS
DOCUMENT NUMBER: 138:297868
TITLE: Percutaneous estrogen in prevention of early **postmenopausal bone loss** in Chinese women
AUTHOR(S): Sun, Aijun; Lin, Shouqing; Yu, Wei; Qin, Mingwei; Chen, Fengling; Zhang, Ying; Wei, Yang; de Lignieres, Bruno

CORPORATE SOURCE: Department of Obstetrics + Gynecology, Peking Union Medical College Hospital, Beijing, 100730, Peop. Rep. China
SOURCE: Chinese Medical Journal (Beijing, China, English Edition) (2002), 115(12), 1790-1795
CODEN: CMJODS; ISSN: 0366-6999
PUBLISHER: Chinese Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objective: To identify the optimal dosage of 17β-estradiol gel + oral progestin for preventing **bone loss** in **postmenopausal** Chinese women. **Methods**: A 3-yr open label, randomized, prospective clin. trial was conducted. Sixty healthy women who had been **postmenopausal** for 1 to 5 yr were recruited and divided into following 4 groups: group 1, percutaneous gel 17β-estradiol (E2) 1.5 mg/d plus micronized progesterone (MP) 100 mg/d; group 2, percutaneous gel 17β-estradiol (E2) 1.5 mg/d plus medroxyprogesterone acetate (MPA) 2 mg/d; group 3, percutaneous gel 17β-estradiol (E2) 0.75 mg/d plus micronized progesterone (MP) 100 mg/d; and group 4, percutaneous gel 17β-estradiol (E2) 0.75 mg/d plus medroxyprogesterone acetate (MPA) 2 mg/d. Estrogen and progestin were given continuously for 25 days per mo. Bone mineral d. (BMD) was measured using quant. computed tomog. (QCT) for trabecular bone of L2-5 and dual energy x-ray absorptiometry (DEXA) for L2-4 and hip at baseline and at 6, 12, 18, 24 and 36 mo visits. Results:98.3% **patients** stayed in the study for 1 yr, 93.3% for 2 yr, and 85% for 3 yr. On average, 80% of **patients** showed relieved **menopausal** symptoms after 6 mo of treatment. By the 24th month, the mean increase in BMD ranged from 4.3% to 7.5% in trabecular bone; and by the 36th month, it ranged from 4.2% to 6.2% in L2-4 and 1.61% to 3.77% in the neck. There were significant difference after treatment ($P < 0.05$). Among the four groups, no significant difference ($P > 0.05$) was found in improvement of symptoms, levels of bone markers or BMD. Conclusion: A daily dose of estradiol gel, either 0.75 mg or 1.5 mg, is effective in preventing early **postmenopausal bone loss** and relieving **menopausal** symptoms. After 3-yr treatment, **spinal** BMD could increase steadily, so does hip BMD, especially in the first 2 yr.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 15 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:927553 HCAPLUS
DOCUMENT NUMBER: 138:13510
TITLE: CDR-grafted anti-**human** p40 antibodies for diagnosis and treatment of conditions mediated by interleukin 12
INVENTOR(S): Peritt, David; Carton, Jill M.
PATENT ASSIGNEE(S): Centocor, Inc., USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002097048	A2	20021205	WO 2002-US16876	20020528
WO 2002097048	A3	20030904		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,
VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG,
KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,
IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG

US 2003157105 A1 20030821 US 2002-156255 20020528
PRIORITY APPLN. INFO.: US 2001-294503P P 20010530

AB The present invention relates to at least one novel anti-p40 or **human** IL-12 Ig-derived protein, including isolated nucleic acids that encode at least one anti-p40 Ig derived protein, IL-12, vectors, host cells, transgenic animals or plants, and **methods** of making and using thereof, including therapeutic compns., **methods** and devices. The **humanized** anti-p40 antibodies and fragments are useful for treating IL-12-mediated diseases.

L11 ANSWER 16 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:907166 HCAPLUS
DOCUMENT NUMBER: 138:322
TITLE: Plasma glucosylceramide deficiency as risk factor for thrombosis and modulator of anticoagulant protein C
INVENTOR(S): Griffin, John H.; Deguchi, Hiroshi; Fernandez, Jose
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 32 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002177563	A1	20021128	US 2002-86943	20020228
US 6756208	B2	20040629		
WO 2002102325	A2	20021227	WO 2002-US6340	20020228
WO 2002102325	A3	20030912		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1370570 A2 20031217 EP 2002-760992 20020228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
US 2004132688 A1 20040708 US 2003-739962 20031217
PRIORITY APPLN. INFO.: US 2001-272103P P 20010228
US 2001-278045P P 20010322
US 2002-86943 A3 20020228
WO 2002-US6340 W 20020228

AB The present invention has determined that exogenously added glucosylceramide (GlcCer) and other neutral glycolipids such as the homologous Glc-containing globotriaosylceramide (Gb3Cer), dose-dependently prolonged clotting times

of normal plasma in the presence but not absence of APC:protein S, indicating GlcCer or Gb3Cer can enhance protein C pathway anticoagulant activity. In studies using purified proteins, inactivation of factor Va by APC:protein S was enhanced by GlcCer alone and by GlcCer, globotriaosylceramide, lactosylceramide, and galactosylceramide in multicomponent vesicles containing phosphatidylserine and phosphatidylcholine. Thus, the present invention provides neutral glycolipids such as GlcCer and Gb3Cer, as anticoagulant cofactors that contribute to the antithrombotic activity of the protein C pathway. The present invention has also determined that a deficiency of plasma GlcCer is a risk factor for thrombosis. **Methods** are provided to determine individuals at risk for thrombosis, **methods** of treatment as well as **methods** of screening for antithrombotic factors from neutral glycolipids.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 17 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:721211 HCAPLUS
DOCUMENT NUMBER: 137:272687
TITLE: Summary of meta-analyses of therapies for **postmenopausal** osteoporosis
AUTHOR(S): Cranney, Ann; Guyatt, Gordon; Griffith, Lauren; Wells, George; Tugwell, Peter; Rosen, Clifford
CORPORATE SOURCE: The Osteoporosis Methodology Group, USA; The Osteoporosis Research Advisory Group
SOURCE: Endocrine Reviews (2002), 23(4), 570-578
CODEN: ERVIDP; ISSN: 0163-769X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. This section summarizes the results of the seven systematic reviews of osteoporosis therapies published in this series [**calcium**, **vitamin D**, **hormone replacement therapy** (HRT), alendronate, risedronate, raloxifene, and calcitonin] and systematic reviews of etidronate and fluoride we have published elsewhere. We highlight the **methodol** . strengths and weaknesses of the individual studies, and summarize the effects of treatments on the risk of vertebral and non-vertebral **fractures** and on **bone** d., including effects in different **patient** subgroups. We provide an estimate of the expected impact of antiosteoporosis interventions in prevention and treatment populations using the number needed to treat (NNT) as a reference In addition to the evidence, judgements about the relative weight that one places on weaker and stronger evidence, attitudes toward uncertainty, circumstances of **patients** ' and societal values or preferences will, and should, play an important role in decision-making regarding anti-osteoporosis therapy.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 18 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:721194 HCAPLUS
DOCUMENT NUMBER: 137:273351
TITLE: Meta-analysis of the efficacy of **hormone replacement therapy** in treating and preventing osteoporosis in **postmenopausal** women
AUTHOR(S): Wells, George; Tugwell, Peter; Shea, Beverley; Guyatt, Gordon; Peterson, Joan; Zytaruk, Nicole; Robinson, Vivian; Henry, David; O'Connell, Diane; Cranney, Ann

CORPORATE SOURCE: The Osteoporosis Methodology Group, USA; The Osteoporosis Research Advisory Group
SOURCE: Endocrine Reviews (2002), 23(4), 529-539
CODEN: ERVIDP; ISSN: 0163-769X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objective: To review the effect of **hormone replacement therapy** (HRT) on **bone** d. and **fractures** in **postmenopausal** women. Data Source: We searched MEDLINE and EMBASE from 1966 to 1999, the Cochrane Controlled Register, citations of relevant articles, and proceedings of international meetings for eligible randomized controlled trials. We contacted osteoporosis investigators to identify addnl. studies, and primary authors for unpublished data. Study Selection: We included 57 studies that randomized **postmenopausal** women to HRT or a control (placebo or **calcium/vitamin D**) and were of at least 1 yr in duration. Seven of these studies reported fractures. Data Abstraction: For each study, three independent reviewers assessed the **methodol.** quality and abstracted the data. Data Synthesis: HRT showed a trend toward reduced incidence of vertebral fractures [relative risk (RR) 0.66, 95% confidence interval (CI) 0.41-1.07; 5 trials] and nonvertebral fractures (RR 0.87, 95% CI 0.71-1.08; 6 trials). HRT had a consistent effect on bone mineral d. (BMD) at all sites. The difference between HRT and control in the percent change in bone d. at 2 yr was 6.76 (5.83, 7.89; 21 trials) at the lumbar **spine** and 4.53 (3.68, 5.36; 14 trials) and 4.12 (3.45, 4.80; 9 trials) at the forearm and femoral neck, resp. Conclusions: HRT has a consistent, favorable and large effect on bone d. at all sites. The data show a nonsignificant trend toward a reduced incidence in vertebral and nonvertebral fractures.

REFERENCE COUNT: 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 19 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:731079 HCAPLUS
DOCUMENT NUMBER: 135:286908
TITLE: Use of androgen receptor gene GGC and CAG repeat polymorphisms for determining osteoporosis susceptibility and/or low bone density
INVENTOR(S): Rousseau, Francois
PATENT ASSIGNEE(S): Signalgene Inc., Can.
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001073116	A2	20011004	WO 2001-CA402	20010328
WO 2001073116	A3	20021212		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,

BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2000-192557P P 20000328
AB The present invention relates to a **method** for determining osteoporosis susceptibility by using genotypes of the androgen receptor gene. More specifically, the present invention relates to two distinct polymorphisms at the AR gene, namely, the CAG repeat coding for a polyglutamine tract and the GGC repeat coding for a polyglycine tract in the 5'part (exon 1) of the AR gene and to a linkage disequil. therebetween which can be correlated with a predisposition to osteoporosis and/or low bone d. and/or high/low bone turnover and/or protection to osteoporosis. The invention further relates to kits for assessing such predispositions and/or protection. As well, the invention relates to osteoporosis susceptibility or to low bone mass, to responsiveness to treatment for osteoporosis, for osteoporosis prognosis or severity, or as a means to classify **patients** in clin. trial for osteoporosis (screening, diagnosis, prognosis or treatment). In addition, the invention relates to assays for screening drugs for osteoporosis or for determining the best treatment for osteoporosis.

L11 ANSWER 20 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:229143 HCAPLUS
DOCUMENT NUMBER: 134:232284
TITLE: **Method** for monitoring treatment with a parathyroid hormone
INVENTOR(S): Hock, Janet M.; Satterwhite, Julie
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 135 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001022093	A1	20010329	WO 2000-US24745	20000911
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2387693	AA	20010329	CA 2000-2387693	20000911
EP 1222465	A1	20020717	EP 2000-961713	20000911
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.:
US 1999-154879P P 19990920
US 1999-156803P P 19990930
US 2000-196370P P 20000412
WO 2000-US24745 W 20000911

AB The present invention relates to a **method** for monitoring effects of administration of a parathyroid hormone by determining levels of one or more markers of an activity of this hormone. Suitable markers of **bone formation** include one or more enzymes indicative of osteoblastic processes of **bone formation**, preferably **bone** specific alkaline phosphatase, and/or one or more products of collagen

biosynthesis, preferably a procollagen I C-terminal propeptide. Suitable markers of bone resorption and turnover include one or more products of collagen degradation, preferably an N-terminal telopeptide (NTX). In addition, **methods** for concurrently reducing the risk of both vertebral and non-vertebral **bone fracture** in a male **human** subject at risk of or having osteoporosis are also disclosed, involving administration of **human parathyroid hormone** (amino acid sequence **1-34**) without concurrent administration of an antiresorptive. **agent** other than **vitamin D** or **calcium.** A kit for monitoring an effect of administration of parathyroid hormone to subject is claimed, as is an article of manufacture comprising **packaging** material and a pharmaceutical composition comprising **human** PTH (1-34) is also claimed.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 21 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:159622 HCAPLUS
DOCUMENT NUMBER: 132:175253
TITLE: Management of corticosteroid-induced osteoporosis
AUTHOR(S): Adachi, Jonathan D.; Olszynski, Wojciech P.; Hanley, David A.; Hodsman, Anthony B.; Kendler, David L.; Siminoski, Kerry G.; Brown, Jacques; Cowden, Elizabeth A.; Goltzman, David; Loannidis, George; Josse, Robert G.; Ste-Marie, Louis-Georges; Tenenhouse, Alan M.; Davison, K. Shawn; Blocka, Ken L. N.; Pollock, A. Patrice; Sibley, John
CORPORATE SOURCE: Department of Medicine, St.Joseph's Hospital, McMaster University, Hamilton, ON, Can.
SOURCE: Seminars in Arthritis and Rheumatism (2000), 29(4), 228-251
CODEN: SAHRBF; ISSN: 0049-0172
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 146 refs. The aim of this study was to educate scientists and health care providers about the effects of corticosteroids on bone, and advise clinicians of the appropriate treatments for **patients** receiving corticosteroids. This review summarizes the pathophysiol. of corticosteroid-induced osteoporosis, describes the assessment **methods** used to evaluate this condition, examines the results of clin. trials of drugs, and explores a practical approach to the management of corticosteroid-induced osteoporosis based on data collected from published articles. Despite our lack of understanding about the biol. mechanisms leading to corticosteroid-induced **bone loss**, effective therapy has been developed. Bisphosphonate therapy is beneficial in both the prevention and treatment of corticosteroid-induced osteoporosis. The data for the bisphosphonates are more compelling than for any other **agent.** For **patients** who have been treated but continue to **lose bone**, **hormone replacement therapy**, calcitonin, fluoride, or anabolic hormones should be considered. **Calcium** should be used only as an adjunctive therapy in the treatment or prevention of corticosteroid-induced **bone loss** and should be administered in combination with other **agents.** Bisphosphonates have shown significant treatment benefit and are the **agents** of choice for both the treatment and prevention of corticosteroid-induced osteoporosis.

REFERENCE COUNT: 146 THERE ARE 146 CITED REFERENCES AVAILABLE FOR

THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L11 ANSWER 22 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:144758 HCAPLUS
DOCUMENT NUMBER: 132:161692
TITLE: **Method** of increasing bone toughness and stiffness and reducing fractures by administering a parathyroid hormone
INVENTOR(S): Hock, Janet M.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000010596	A1	20000302	WO 1999-US18961	19990819
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2325371	AA	20000302	CA 1999-2325371	19990819
AU 9955750	A1	20000314	AU 1999-55750	19990819
AU 746277	B2	20020418		
BR 9909445	A	20001212	BR 1999-9445	19990819
EP 1059933	A1	20001220	EP 1999-942350	19990819
EP 1059933	B1	20030115		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200003455	T2	20010621	TR 2000-200003455	19990819
EP 1136076	A1	20010926	EP 2001-202735	19990819
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002523375	T2	20020730	JP 2000-565916	19990819
AT 231000	E	20030215	AT 1999-942350	19990819
EP 1295605	A2	20030326	EP 2002-79227	19990819
EP 1295605	A3	20031029		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
ES 2190244	T3	20030716	ES 1999-942350	19990819
NZ 507056	A	20031031	NZ 1999-507056	19990819
TW 576747	B	20040221	TW 1999-88114185	19991026
ZA 2000004993	A	20011219	ZA 2000-4993	20000919
HR 2000000755	A1	20010228	HR 2000-755	20001106
NO 2000005947	A	20001124	NO 2000-5947	20001124
HK 1030545	A1	20030711	HK 2001-101056	20010214

PRIORITY APPLN. INFO.:

US 1998-97151P	P	19980819
US 1998-99746P	P	19980910
EP 1999-942350	A3	19990819
WO 1999-US18961	W	19990819

AB The invention relates to a **method** for increasing the toughness

and/or stiffness of bone and/or reducing the likelihood and/or severity of **bone fracture** by administering a parathyroid hormone. The **method** can be employed to increase toughness or stiffness of bone at a site of a potential or actual trauma, such as the hip or **spine** of a person at risk of or suffering from osteoporosis. The **method** of the invention can reduce the incidence of vertebral fracture, reduce the incidence of multiple vertebral fractures, reduce the severity of vertebral fracture, and/or reduce the incidence of non-vertebral fracture.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 23 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:46743 HCAPLUS
DOCUMENT NUMBER: 132:88752
TITLE: Osteopenia in young **hypogonadal** women with systemic lupus erythematosus receiving chronic steroid therapy: a randomized controlled trial comparing calcitriol and hormonal replacement therapy
AUTHOR(S): Kung, A. W. C.; Chan, T. M.; Lau, C. S.; Wong, R. W. S.; Yeung, S. S. C.
CORPORATE SOURCE: Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong, Peop. Rep. China
SOURCE: Rheumatology (Oxford) (1999), 38(12), 1239-1244
CODEN: RUMAFK; ISSN: 1462-0324
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objective. To evaluate the efficacy of calcitriol and hormonal replacement therapy (HRT) in the treatment of steroid-induced osteoporosis in **hypogonadal** women. **Methods.** We studied 28 young **patients** (**aged** 37±6 yr) with systemic lupus erythematosus (SLE) on chronic steroid therapy for 130±22 mo and requiring more than 10 mg/day prednisone. They were amenorrhoeic for more than 2 yr with proven ovarian failure. All had osteopenia with a T score at L2-4 of less than -1. They were randomized to receive HRT (conjugated estrogen 0.625 mg daily from day 1 to day 21 plus medroxyprogesterone acetate 5 mg daily days 10-21) or calcitriol 0.5 μg daily. All received **calcium** carbonate 1 g/day. Results. There were no differences in the baseline demog., bone mineral d. (BMD) and biochem. data between the two groups. Lumbar **spine** BMD increased by 2.0±0.4% after 2 yr with HRT ($P < 0.05$), but reduced by 1.74±0.4% ($P < 0.05$) with calcitriol treatment. No change was seen at the distal one-third radius with HRT treatment but significant **bone loss** (2.3±1.4%, $P < 0.02$) was observed with calcitriol therapy. BMD at the hip did not change in both groups. Comparing both treatment groups, significant differences in the BMD at the **spine** ($P < 0.03$) and radius ($P < 0.05$) were seen at the end of 2 yr. The changes in urinary n-telopeptide excretion but not serum osteocalcin at 6 mo and 12 mo were inversely correlated with the changes in lumbar **spine** BMD at 24 mo. HRT did not cause an adverse effect on SLE disease activity. Conclusion. HRT but not calcitriol could prevent **bone loss** in young **hypogonadal** women on chronic steroid therapy.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 24 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:520424 HCAPLUS
DOCUMENT NUMBER: 131:165442

TITLE: Transdermal progesterone cream for vasomotor symptoms and **postmenopausal bone loss**
AUTHOR(S): Leonetti, Helene B.; Longo, Santo; Anasti, James N.
CORPORATE SOURCE: Departments of Obstetric and Gynecology and Pathology, St. Luke's Hospital, Bethlehem, PA, USA
SOURCE: Obstetrics & Gynecology (New York) (1999), 94(2), 225-228
CODEN: OBGNAS; ISSN: 0029-7844
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objective: To determine effectiveness of transdermal progesterone cream for controlling vasomotor symptoms and preventing **postmenopausal bone loss. Methods**: We randomly assigned 102 healthy women within 5 yr of **menopause** to transdermal progesterone cream or placebo. Study subjects and investigators were masked until data anal. was completed. An initial evaluation included complete history, phys. examination, bone mineral d. determination, and serum studies (TSH, FSH, lipid profile, and chemical profile). Subjects were instructed to apply a quarter tsp of cream (containing 20 mg progesterone or placebo) to the skin daily. Each woman received daily multivitamins and 1200 mg of **calcium** and were seen every 4 mo for review of symptoms. Bone scans and serum chemistries were repeated after 1 yr. Results: Thirty of the 43 (69%) in the treatment group and 26 of the 47 (55%) in the placebo group complained initially of vasomotor symptoms. Improvement or resolution of vasomotor symptoms, as determined by review of weekly symptom diaries, was noted in 25 of 30 (83%) treatment subjects and five of 26 (19%) placebo subjects ($P < .001$). However, the number of women who showed gain in bone mineral d. exceeding 1.2% did not differ ($\alpha = .05$, power of 80%). Conclusion: Although we found no protective effect on bone d. after 1 yr, we did see a significant improvement in vasomotor symptoms in the treated group.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 25 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:129471 HCAPLUS
DOCUMENT NUMBER: 130:295053
TITLE: Urinary bone resorption markers in monitoring treatment of symptomatic osteoporosis
AUTHOR(S): Parviainen, Markku T.; Jaaskelainen, Kalle; Kroger, Heikki; Arnala, Ilkka; Alhava, Esko
CORPORATE SOURCE: Department of Clinical Chemistry, Kuopio University Hospital, Kuopio, FIN-70210, Finland
SOURCE: Clinica Chimica Acta (1999), 279(1-2), 145-154
CODEN: CCATAR; ISSN: 0009-8981
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have studied the clin. usefulness of urinary bone resorption markers in **postmenopausal** women with symptomatic osteoporosis. The study design is a randomized double-blind placebo controlled study, in which the subjects were daily treated for 24 mo either with a hormone analog (2.5 mg Livial, generic name Tibolone, Organon, Amsterdam, Holland) plus 800 mg **calcium** (**age** 63 yr, range 52-68 yr), or with placebo plus 800 mg **calcium** (**age** 66 yr, range 50-75 yr). The laboratory **methods** for urinary bone resorption markers were enzyme immunoassays (EIA) for urinary pyridoline (PYD) and

deoxypyridoline crosslinks (DPD), and for cross-linked N-telopeptides of type I Collagen (NTx), and an HPLC assay for urinary hydroxyproline (HOP). All the urine assay results were calculated per mmol creatinine. All the resorption markers decreased during the two-year study period in both groups. The Z scores (discriminating power, i.e., ability of the different tests to distinguish the hormone treated subjects from the placebo treated subjects) for HOP and PYD were rather low: 0.06-1.52 for HOP and 0.68-1.47 for PYD. The differences between the two treatment groups were statistically significant for DPD at 12 and 24 mo of treatment, the Z scores ranging 0.45-1.90. NTx showed the most prominent decrease from the beginning of the study especially in the hormone treatment group: the differences between the two treatment groups were highly statistically significant for NTx already at 6 mo of treatment, and the Z scores remained high ranging 2.11-3.82 throughout the two-year study period. Dual x-ray absorptiometry (DXA) of the lumbar **spine** and femoral neck did not show differences between the two treatment groups throughout the two-year study period. After 2 yr, there was, however, a significant increase in bone d. both in the **spine** (+ 6.6%) and in the femoral neck (+ 3.4%) in the women with hormone treatment. In the control group a significant increase (+ 5.1%) in the **spine**, whereas a non-significant decrease in the femoral neck was observed Thus, measurement of urinary cross-linked peptides derived from type I collagen (NTx and DPD) might be a useful biochem. **method** of observing the pos. clin. effect, i.e., reduction in bone resorption, following **hormone replacement therapy** in **postmenopausal** fracture **patients.**

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 26 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:764297 HCAPLUS
DOCUMENT NUMBER: 130:25345
TITLE: Preparation of cyclic peptide parathyroid hormone analogs
INVENTOR(S): Condon, Stephen M.; Morize, Isabelle
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 188 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9851324	A1	19981119	WO 1998-US9843	19980513
W: AL, AM, AU, BA, BB, BR, CA, CH, CU, CZ, EE, ES, FI, GB, GH, HU, IL, IS, KP, LC, LK, LR, LT, LU, MG, MK, MX, NO, PT, RO, RU, SD, SI, SK, TT, UA, US, VN, AM, AZ, TJ, TM				
RW: GH, GM, KE, LS, MW, SZ, UG, BE, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, CI, GA, MR, SN, TD, TG				
CA 2290443	AA	19981119	CA 1998-2290443	19980513
AU 9873867	A1	19981208	AU 1998-73867	19980513
AU 746461	B2	20020502		
EP 986395	A1	20000322	EP 1998-921200	19980513
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
BR 9808786	A	20000711	BR 1998-8786	19980513
JP 2001517957	T2	20011009	JP 1998-549536	19980513
ZA 9804077	A	19981124	ZA 1998-4077	19980514

US 6472505	B1	20021029	US 1999-228990		19990112
NO 9905568	A	19991229	NO 1999-5568		19991112
US 2002132973	A1	20020919	US 2002-97079		20020313
PRIORITY APPLN. INFO.:			US 1997-46472P	P	19970514
			WO 1998-US9843	W	19980513
			US 1999-228990	A3	19990112

OTHER SOURCE(S): MARPAT 130:25345

AB This invention is directed to cyclic and acyclic analogs of **human parathyroid hormone**(1-34) [**hPTH**(1-34)] and **human parathyroid hormone**-related protein(1-34) [**hPTHrP**(1-34)], to pharmaceutical compns. comprising these peptide compds., and to a **method** of treating diseases associated with **calcium** regulation in the body. Thus, cyclo(Lys18-Asp22)[Ala1,Nle8,Lys18,Asp22,Leu27]**hPTH**(1-31)-NH2 (I) was prepared by solid-phase **methods** on a Ring amide MBHA resin and 9-fluorenylmethoxycarbonyl (Fmoc) Nα-protection. I showed activity in a ROS 17.2/8 cell cAMP assay.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 27 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:677238 HCAPLUS

DOCUMENT NUMBER: 127:341966

TITLE: Raloxifene and estrogen: comparative bone-remodeling kinetics

AUTHOR(S): Heaney, Robert P.; Draper, Michael W.

CORPORATE SOURCE: Creighton University, Omaha, NE, 68178, USA

SOURCE: Journal of Clinical Endocrinology and Metabolism (1997), 82(10), 3425-3429
CODEN: JCEMAZ; ISSN: 0021-972X

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The pattern of changes in **human** bone remodeling produced by raloxifene (60 mg/day) was compared to that of estrogen (given as **hormone replacement therapy**) in 33 early **postmenopausal** women randomly assigned to raloxifene, estrogen, or no treatment. Remodeling was measured using **calcium** tracer kinetic **methods** employed under a constant diet and full metabolic balance conditions. Studies were performed at baseline and, to detect both early and late remodeling changes, at 4 and 31 wk of treatment. Both raloxifene and estrogen produced a significant pos. **calcium** balance shift at each treatment measurement point: +74 and +60 mg/day at 4 wk, and +60 and +91 mg/day at 31 wk for raloxifene and estrogen, resp. Externally, this balance change was due to a highly significant fall in the urinary **calcium** level and marginal improvement in **calcium** absorption efficiency. Internally, bone resorption was significantly reduced at both measurement points: -64 and -60 mg/day at 4 wk, and -82 and -162 mg/day at 31 wk for raloxifene and estrogen, resp. **Bone formation** was not significantly affected by either **agent** at 4 wk; at 31 wk, formation was reduced by estrogen, but not by raloxifene. Thus, at 4 wk, the general pattern of remodeling change was identical for the two **agents.** At 31 wk, remodeling suppression was greater for estrogen than for raloxifene; however, remodeling balance was the same for the two **agents.** We conclude that raloxifene and estrogen affect the bone remodeling apparatus similarly, and that raloxifene, therefore, is acting on bone as an estrogen agonist.

L11 ANSWER 28 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1981:474268 HCAPLUS
DOCUMENT NUMBER: 95:74268
TITLE: Treatment with **human parathyroid hormone** fragment (**hPTH 1-34**) stimulates **bone formation** and intestinal **calcium** absorption in the greyhound: comparison with data from the osteoporosis trial
AUTHOR(S): Podbesek, R. D.; Stevenson, R.; Zanelli, G. D.; Edouard, C.; Meunier, P. J.; Reeve, J.; Parsons, J. A.
CORPORATE SOURCE: Natl. Inst. Med. Res., London, NW7, UK
SOURCE: International Congress Series (1981), Volume Date 1980, 511(Horm. Control Calcium Metab.), 118-23
CODEN: EXMDA4; ISSN: 0531-5131
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The pulsatile s.c. administration of **human** parathyroid hormone1-34 (PTH) [**52232-67-4**] to greyhounds was more effective than continuous s.c. infusion in stimulating osteoid **formation** in **bone** as well as in stimulating **Ca** absorption and **Ca** skeletal accretion. Both **methods** of administration had similar effects on bone resorption surfaces. The osteoclast count was elevated to the same extent by both **methods** of administration. A single daily injection of PTH markedly increased **Ca** intestinal absorption in dogs in contrast to results found in **postmenopausal** osteoporosis **patients.** The greyhound appears to be a useful model for understanding **human Ca** metabolism and cellular biol. of bones.

```
=> d que stat l19
L1             1 SEA FILE=REGISTRY ABB=ON  "HPTH-(1-34)"/CN
L2             1 SEA FILE=REGISTRY ABB=ON  "VITAMIN D"/CN
L3             1 SEA FILE=REGISTRY ABB=ON  CALCIUM/CN
L4        161514 SEA FILE=HCAPLUS ABB=ON  (?BONE?(3A)(?FRACT? OR ?FORM? OR
                 ?LOSS? OR ?LOSE?) OR ?OSTEPOROSIS? OR ?OSTEOGENESIS? OR
                 ?SPINE? OR ?SPINAL?)
L5          1004 SEA FILE=HCAPLUS ABB=ON  L4 AND (L1 OR HPTH(W)(1-34) OR ?HPTH?
                 OR ?HUMAN?(W)?PARATHYROID?(W)?HORMONE?(3W)(1-34) OR ?HORMONE?(W
                 )?REPLACEMENT?(W)?THERAPY?)
L6           300 SEA FILE=HCAPLUS ABB=ON  L5 AND (L2 OR L3 OR ?VITAMIN?(W)D OR
                 CA OR ?CALCIUM?)
L7           229 SEA FILE=HCAPLUS ABB=ON  L6 AND (AGE? OR ?AGING? OR ?GERIAT?
                 OR ?SENIL? OR ?MENOPAUS? OR ?KLINEFELTER?(W)?SYNDROM? OR
                 ?HYPOGONAD? OR ?GONAD?(W)?DISORDER?)
L8           168 SEA FILE=HCAPLUS ABB=ON  L7 AND (?HUMAN? OR ?PATIENT?)
L9             2 SEA FILE=HCAPLUS ABB=ON  L8 AND (?REDUCE? OR ?LESSEN? OR
                 ?CONTROL? OR ?DECREAS?)(W)?RISK?
L10          168 SEA FILE=HCAPLUS ABB=ON  L8 OR L9
L11           28 SEA FILE=HCAPLUS ABB=ON  L10 AND (?METHOD? OR ?TECHNIQ?)
L12          343 SEA L11
L13          241 DUP REMOV L12 (102 DUPLICATES REMOVED)
L14           67 SEA L13 AND (MONITOR? OR DETECT? OR DETERMIN?)
L15            1 SEA L14 AND HPTH(W)(1-34)
L16            1 SEA L14 AND ?HUMAN?(W) ?PARATHYROID?(W) ?HORMON?(W)(1-34)
L17            1 SEA L15 OR L16
L18            7 SEA L14 AND ?GONAD?
L19            8 SEA L17 OR L18

=> d ibib abs l19 1-8

L19  ANSWER 1 OF 8     MEDLINE on STN
ACCESSION NUMBER:    2004358374      IN-PROCESS
DOCUMENT NUMBER:     PubMed ID: 15262455
TITLE:               Teriparatide: a review.
AUTHOR:              Quattrocchi Elaena; Kourlas Helen
CORPORATE SOURCE:    Pharmacy Practice Department, Arnold and Marie Schwartz
                     College of Pharmacy and Health Sciences, Long Island
                     University, Brooklyn, New York 11201-5497, USA.
SOURCE:              Clinical therapeutics, (2004 Jun) 26 (6) 841-54.
                     Journal code: 7706726. ISSN: 0149-2918.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE:          Entered STN: 20040721
                     Last Updated on STN: 20040723
AB   BACKGROUND: Traditionally, the management of osteoporosis in men and women
     has included the use of antiresorptive agents in combination
     with calcium and vitamin D supplementation.
     The mechanism of action of teriparatide is unique in that it possesses
     anabolic properties and therefore builds bone.  Since the approval of
     teriparatide in the United States in 2002, a great deal of interest
     regarding its use in osteoporosis has developed.  OBJECTIVES: This article
     reviews the information available on the new recombinant human
     parathyroid hormone teriparatide (hPTH [
     1-34]), including its clinical pharmacology, mechanism
     of action, pharmacokinetic properties, clinical efficacy, safety profile,
     potential drug interactions, contraindications and warnings, dosage and
     administration, and pharmacoeconomics.  METHODS: The articles
```

included in this review were identified through searches of PubMed and MEDLINE (1966-December 2003) and International Pharmaceutical Abstracts (1970-December 2003). Search terms included teriparatide, Forteo, recombinant **human parathyroid hormone** (**1-34**), and osteoporosis. The references of the identified articles were reviewed for additional publications. Specific product information was also obtained from the manufacturer of teriparatide. RESULTS: Teriparatide has been studied in **postmenopausal** women with osteoporosis, drug-induced osteoporosis (specifically, corticosteroid-induced osteoporosis), and men with osteoporosis. The data available from various clinical trials have shown an increase in both bone mineral density (BMD) and bone mineral content (BMC) with the use of teriparatide compared with placebo. One study found that women treated with the 20-microg dose and the 40-microg dose were 35% and 40%, respectively, less likely to have one or more new nonvertebral fractures compared with placebo ($P = 0.02$). Another study compared the use of daily teriparatide 40-microg injections versus oral daily alendronate. Results showed that the incidence of nonvertebral fractures was significantly lower in the teriparatide group than the alendronate group ($P < 0.05$). A study using 20- and 40-microg daily injections of teriparatide was performed in men with osteoporosis. There was a statistically significant increase in lumbar **spine** BMD of 5.9% in the 20-microg group and 9.0% in the 40-microg group (both, $P < 0.001$). In the femoral neck, a 1.5% increase in BMD occurred in the 20-microg group ($P = 0.021$) and a 0.9% increase in the 40-microg group ($P < 0.001$). A limited number of studies are available assessing the combination of antiresorptive medications and teriparatide; however, the available data suggest that the effects of teriperatide do not require prior stimulation of bone resorption. CONCLUSIONS: Teriparatide has been shown clinically to improve BMD and BMC in **postmenopausal** women and in men. Because of its anabolic capabilities, teriparatide can be used as an alternative to the traditional therapies that are currently available for the treatment of osteoporosis, with scheduled **monitoring** for adverse effects such as hypercalcemia and urinary **calcium** excretion. In 1 study, mild hypercalcemia was seen most often 4 to 6 hours after SC injection of teriparatide before returning to normal. Urinary **calcium** was observed to increase by 30 mg/d (0.75 mmol/d) with teriparatide.

L19 ANSWER 2 OF 8 MEDLINE on STN
ACCESSION NUMBER: 96378606 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8784169
TITLE: Osteoporosis prevention and treatment.
AUTHOR: Bellantoni M F
CORPORATE SOURCE: Division of Geriatric Medicine, Johns Hopkins Medical School, Baltimore, MD, USA.
SOURCE: American family physician, (1996 Sep 1) 54 (3) 986-92, 995-6. Ref: 31
Journal code: 1272646. ISSN: 0002-838X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961022
Last Updated on STN: 19961022
Entered Medline: 19961004

AB Bone fragility resulting from osteoporosis places a significant percentage

of elderly women and other **patient** groups at risk for **bone fracture.** Risk factors for osteoporosis include **hypogonadal** states (particularly **menopause**), smoking, low **calcium** intake, lack of weight-bearing exercise, family history and use of certain medications. Preventive strategies are based on achieving and maintaining optimal bone mass through diet, exercise, appropriate use of **hormone replacement therapy** and avoidance of adverse influences, particularly smoking and certain medications. Laboratory investigations are of limited use in the **detection** and assessment of osteoporosis, but new **techniques** may help physicians identify **patients** with accelerated bone metabolism. Currently, the most precise **method** of radiologically assessing osteoporosis is dual-energy x-ray absorptiometry. Many new **agents** for the treatment of osteoporosis are being examined. First-line therapies currently include alendronate and calcitonin. The choice of therapy must be individualized and combined with advice about nutrition and exercise, both to optimize bone density and to minimize the risk of trauma.

L19 ANSWER 3 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:235719 BIOSIS
DOCUMENT NUMBER: PREV200200235719
TITLE: The role of tacrolimus (FK506)-based immunosuppression on bone mineral density and bone turnover after cardiac transplantation: A prospective, longitudinal, randomized, double-blind trial with calcitriol.
AUTHOR(S): Stempfle, Hans-Ulrich [Reprint author]; Werner, Christiane; Siebert, Uwe; Assum, Tanja; Wehr, Uli; Rambeck, Walter A.; Meiser, Bruno; Theisen, Karl; Gartner, Roland
CORPORATE SOURCE: Department of Cardiology, Medizinische Klinik, Klinikum Innenstadt, Ludwig-Maximilians University, Ziemssenstrasse 1, 80336, Munich, Germany
SOURCE: Transplantation (Baltimore), (February 27, 2002) Vol. 73, No. 4, pp. 547-552. print.
CODEN: TRPLAU. ISSN: 0041-1337.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Apr 2002
Last Updated on STN: 10 Apr 2002

AB Background: Tacrolimus (FK506) is a new immunosuppressive drug in organ transplantation that has demonstrated experimentally to be more deleterious on bone mineral metabolism than cyclosporine. The purpose of this clinical study was to evaluate the effects of a tacrolimus-based immunosuppression on the skeleton and to investigate in a prospective, longitudinal, randomized, double-blind, study the effect of 0.25 mug calcitriol (1,25-dihydroxyvitamin D3) versus placebo in the prevention of **bone loss** and **fracture** rate after heart transplantion (HTx). **Methods**: A total of 53 **patients** (5 female, 48 male, mean **age**: 53+-11 years) were randomized to the study medication. Basic therapy included **calcium** and sex hormone replacement in **hypogonadism.** Bone mineral density of the lumbar **spine** (LS) and femoral neck (FN) were performed at baseline, after 12 and 24 months. Biochemical indexes of mineral metabolism were measured every 3 months. Results: Overall bone mineral density (BMD) was significantly decreased after HTx (T-score-LS: 89+-13%; FN: 88+-14%). LS-BMD (% change in g/cm2) increased significantly within the study period in the calcitriol group (12 months: 7.1+-8.1%, P<0.01; 24 months: 14.0+-10.1%, P<0.01) and showed a positive trend in the placebo group (12 months: 4.5+-9.3%, NS; 24 months: 6.2+-8.0%, NS). FN-BMD in the calcitriol group was stable (12 months: -2.1+-4.2%; NS; 24 months:

-0.9+-3.2%, NS). FN-BMD in the placebo group decreased significantly within the first 12 month follow-up period (-7.3+-5.4; P<0.05) and stabilized within 2 years (-8.0+-4.1%; P<0.05). Fracture incidence was low during the study interval (first year: 5.0%, second year: 0%). Bone resorption markers decreased significantly during calcitriol therapy. Conclusions: High dose tacrolimus-based immunosuppressive regimen is associated with a rapid **bone loss** early after cardiac transplantation. Beyond the first 6 months after HTx, **calcium**, **vitamin D**, and hormone supplementation in **hypogonadism** lead sufficiently to bone mineral recovery. Besides immunosuppression, both concomitant **hypogonadism** and secondary hyperparathyroidism play a major role for the **bone loss** and should be therefore **monitored** and treated adequately. Low dose calcitriol should be substituted for at least 2 years as additional antiresorptive therapy.

L19 ANSWER 4 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2001:308406 BIOSIS
DOCUMENT NUMBER: PREV200100308406
TITLE: Longitudinal evaluation of the contribution of **hypogonadism** to the severity of osteoporosis in homozygous beta-thalassemia.
AUTHOR(S): Chatterjee, R. [Reprint author]; Gemidjioglu, M. E.; Davis, B. A.; Helal, M. A.; Cullum, I.; Porter, J. B.
CORPORATE SOURCE: Department of Reproductive Medicine, University College, London, UK
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 2, pp. 23b. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Jun 2001
Last Updated on STN: 19 Feb 2002

AB With increased longevity in homozygous beta thalassemias (HbetaT) osteopenia-osteoporosis has emerged as a serious problem, impairing quality of life. In cross sectional studies, underproduction of sex steroids secondary to **hypogonadotrophic hypogonadism** (HH) has been shown to play an important role. If HH is the predominant etiology, then timely use of **hormone replacement therapy** (HRT) should be as effective as in **patients** with osteopenia resulting only from underproduction of sex steroids, such as in premature ovarian failure (POF). We therefore examined the longitudinal effects of HRT (parenteral testosterone (TRT) in males and oral cyclical estrogen (ERT) in females) on bone density (BMD) in 92 **patients** with HbetaT (F=50, M=42) over a 15 year period. BMD responses to HRT in females with HbetaT (median follow up 7 yrs) were compared with responses of 375 non-thalassemic women with POF receiving HRT for a median of 8yrs. BMD of the lumbar **spine** and femur were **determined** by dual energy X-ray absorptiometry. Osteoporosis and osteopenia were defined according to the WHO criteria (BMD >2.5SD and >1SD respectively below the peak bone mass in healthy controls, expressed as the T score). We also analyzed the relative influence of other factors including serum ferritin and polymorphisms in 3 candidate genes associated with osteoporosis; type 1 collagen, estrogen receptor and **vitamin D** receptor genes. Females with HbetaT were severely osteopenic, particularly in the **spine**, (mean **spinal** T score =

-0.79+-0.52). In acycling females with HbetaT (n=36), mean **spinal** BMD was markedly lower (T score = -2.26+-0.17) than in the cycling group (n=14) (T = -1.7+-0.34, P<0.05). The acycling females with HbetaT also responded poorly to ERT (pre treatment **spinal** T =-0.75+-0.02 vs -0.68+-0.10 post treatment). By contrast, POF **patients** responded to HRT favorably (pre ERT **spinal** T = -0.88+-0.2 vs post ERT = -0.094+-0.02, P< 0.001). Male thalassemics were also severely osteopenic (**spinal** BMD T score = -0.75+-1.2) but there was no difference in the BMD between males with spontaneous puberty (T = -0.75+-0.3, n=13) and those with HH (T = -0.78+-0.8, n=29). TRT produced a good response in the males (**spinal** T score, pre HRT = -0.77+-0.3 vs -0.083+-0.2 post HRT, P<0.001). There was no association between the degree of osteopenia and the 3 candidate genes, serum ferritin and **age** of onset of chelation in both sexes. These findings show the importance of HH to osteopenia in females with HbetaT. However the poor response of these females to ERT could indicate relative target organ resistance to estrogen in HbetaT.

L19 ANSWER 5 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1999:517948 BIOSIS
DOCUMENT NUMBER: PREV199900517948
TITLE: Prevention of osteoporosis after cardiac transplantation. A prospective, longitudinal, randomized, double-blind trial with calcitriol.
AUTHOR(S): Stempfle, Hans-Ulrich [Reprint author]; Werner, Christiane; Echtler, Sylvia; Wehr, Uli; Rambeck, Walter A.; Siebert, Uwe; Ueberfuhr, Peter; Angermann, Christiane E.; Theisen, Karl; Gaertner, Roland
CORPORATE SOURCE: Department of Cardiology, Medizinische Klinik, Klinikum Innenstadt, Ludwig-Maximilians University, Ziemssenstrasse 1, 80336, Munich, Germany
SOURCE: Transplantation (Baltimore), (Aug. 27, 1999) Vol. 68, No. 4, pp. 523-530. print.
CODEN: TRPLAU. ISSN: 0041-1337.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Dec 1999
Last Updated on STN: 3 Dec 1999

AB Background: Accelerated **bone loss** is a well-recognized complication after cardiac transplantation (HTx) due to immunosuppressive therapy. The purpose of this prospective, longitudinal, randomized, placebo-controlled, double-blind study was to investigate the effect of calcitriol (1,25-dihydroxyvitamin D3) in the prevention of **bone loss** and **fracture** rate after HTx. **Methods**: Basic therapy included 1000 mg of **calcium** daily and sex hormone replacement in **hypogonadal patients.** A total of 132 **patients** (111 male, 21 female; mean **age**: 51+-10 years; 35+-25 months after HTx) were randomized to 0.25 mug of calcitriol or placebo. Bone mineral density (BMD, g/cm2; T score, %) of the lumbar **spine** and x-rays for the assessment of vertebral fractures were performed at baseline and after 12, 24, and 36 months. Biochemical indexes of mineral metabolism were measured every 3 months. Results: Overall BMD was significantly decreased after HTx (T score 87+-13%). BMD increased continuously within the studyperiod in the calcitriol group (1 year: 2.2+-4.8%; 2 years: 3.9+-5.4%; 3 years: 5.7+-4.4%) as well as in the placebo group (1 year: 1.8+-4.9%; 2 years: 3.7+-6.5%; 3 years: 6.1+-7.8%) without statistical difference between the groups. Fracture incidence was low during the study interval (1 year: 2.0%; 2 years: 3.4%; 3 years: 0%). **Hypogonadism** (20%) was associated with a lower BMD (78+-12% vs. 88+-12%; P<0.01) and a higher increase (35%) after hormone replacement in

comparison to **normogonadal patients.** Increased intact parathyroid hormone and bone resorption markers decreased significantly during therapy. Conclusions: **Calcium** supplementation and sex hormone replacement in **hypogonadism** proved a sufficient long-term prevention therapy to improve decreased BMD and to prevent fractures after HTx. Besides immunosuppression, both concomitant **hypogonadism** and secondary hyperparathyroidism play a major role in the long-term **bone loss** and should therefore be **monitored** and treated adequately. Low-dose calcitriol demonstrated no significant extra benefit regarding BMD and fracture rate in the long-term period after HTx.

L19 ANSWER 6 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1999:316251 BIOSIS
DOCUMENT NUMBER: PREV199900316251
TITLE: Bone mineral density of **patients** with thalassemia major: Four-year follow-up.
AUTHOR(S): Molyvda-Athanasopoulou, E. [Reprint author]; Sioundas, A.; Karatzas, N.; Aggellaki, M.; Pazaitou, K.; Vainas, I.
CORPORATE SOURCE: Aristotelian University of Thessaloniki, Thessaloniki, 54006, Greece
SOURCE: Calcified Tissue International, (June, 1999) Vol. 64, No. 6, pp. 481-484. print.
CODEN: CTINDZ. ISSN: 0171-967X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Aug 1999
Last Updated on STN: 17 Aug 1999

AB The purpose of this study was to evaluate the bone mineral density (BMD) of 50 **patients aged** 9-28 years, with thalassemia major and to assess the alterations of bone density in a 4-year follow-up study. They were measured with a DPX densitometer at the lumbar **spine** and femur area and divided into three groups: preadolescents, adolescents, and adults. All **patients** received **calcium** and **vitamin D** supplements, and 8 of the 50 received **hormone replacement therapy** (HRT). All **patients** had a significantly lower BMD compared with healthy subjects. Mean values of lumbar BMD of the three groups were 1.3, 2, and 3 standard deviations (SDs) lower than those of healthy subjects of the same **age.** All adolescent **patients** with normal **gonadal** function and those who received HRT showed an increase in BMD during the period of the study. Adult **patients** also showed an increase in bone density as long as the treatment lasted. However, adolescent and adult **patients** who had **hypogonadotropic hypogonadism** but could not get therapy showed a decrease in bone density. BMD of **patients** with thalassemia major shows a good index of bone status which should be evaluated, especially for the **determination** and follow-up of therapy.

L19 ANSWER 7 OF 8 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2000158095 EMBASE
TITLE: Use of quantitative ultrasound densitometry in male osteoporosis: Diagnosis and treatment.
AUTHOR: Wuster C.; Hadji P.
CORPORATE SOURCE: Dr. C. Wuster, University of Heidelberg, Department of Internal Medicine I, Ingrimstr. 30, D-69117 Heidelberg, Germany
SOURCE: Aging Male, (1999) 2/4 (228-239).
Refs: 43

ISSN: 1368-5538 CODEN: AGMAF7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
020 Gerontology and Geriatrics
027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Male osteoporosis has a prevalence of around 5% (vertebral fractures). Secondary causes such as gastrointestinal diseases with malabsorption, alcoholism and malignant diseases are common. **Hypogonadism** is often not diagnosed since clinical signs are subtle. Diagnosis of osteoporosis is made using clinical history (risk factors), clinical examination (e.g. reduction of stature, back pain), X-ray, densitometry and laboratory work-up. Cut-off values for the WHO classification of male osteoporosis and all densitometry **techniques**, such as dual-energy X-ray absorptiometry (DXA), quantitative ultrasound (QUS) and quantitative computed tomography (QCT), need to be developed. QUS can be measured at the calcaneus and phalanges. Phalangeal ultrasound is especially useful because it is easily accessible, fast, radiation-free, portable and cheap. Preliminary results show that phalangeal ultrasound may **detect** structural deterioration, especially in **patients** on glucocorticoid treatment, earlier than **spinal** DXA. The prevention of osteoporosis is based on the intake of **calcium** and **vitamin D** or its analogs. In **hypogonadal** men, or in men with osteoporosis with low-to-normal or decreased testosterone levels, the use of **hormone replacement therapy** with testosterone for at least 10 years, with yearly andrological examination and prostate ultrasonography, will lead to a significant increase of bone density. Bisphosphonates inhibit osteoclastic bone resorption and are the most effective treatment with regards to **fracture** reduction. **Bone-forming** drugs, such as fluoride or anabolic steroids, can activate osteoblasts; however, reduction in fracture incidence has not been shown. Parathyroid hormone, growth hormone and selective estrogen receptor modulators (SERMs) are prospective treatments for the future.

L19 ANSWER 8 OF 8 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 77121661 EMBASE
DOCUMENT NUMBER: 1977121661
TITLE: Body composition and skeletal metabolism following pituitary irradiation in acromegaly.
AUTHOR: Aloia J.F.; Petrak Z.; Ellis K.; Cohn S.H.
CORPORATE SOURCE: Dept. Med., Nassau County Med. Cent., East Meadow, N.Y. 11554, United States
SOURCE: American Journal of Medicine, (1976) 61/1 (59-63). CODEN: AJMEAZ
DOCUMENT TYPE: Journal
FILE SEGMENT: 003 Endocrinology
014 Radiology
023 Nuclear Medicine
006 Internal Medicine
LANGUAGE: English
AB The change in body composition in acromegaly which resulted from pituitary irradiation was examined using the technic of total body neutron activation analysis. Before treatment, increased ratios of total body P:

Ca, P:K and Na:K were noted. After pituitary irradiation, the total body levels of P, Na and K were reduced in a proportion that indicated restoration of body composition towards normal. Skeletal mass (total body **calcium**) decreased into the range observed in osteoporosis in several **patients.** Trabecular bone mass, as reflected by the Singh Index, was consistently reduced, and two **patients** had vertebral compression **fractures.** Local **bone** mass as **determined** by photon absorptiometry was reduced when the values were normalized for **age**, sex and body size. It is postulated that in untreated acromegaly there is differential bone remodelling with an increase in cortical bone accompanied by a reduced trabecular bone mass. When reduction of hGH levels is accomplished with treatment, cortical apposition may decrease. Since the increased cortical bone mass probably aids in preventing vertebral compression fractures, the treated acromegalic **patient** may incur an increased risk of fractures. This risk may be increased further by the **hypogonadism** which may arise secondary to pituitary irradiation or surgery. It would be prudent to ensure that the **hypogonadal** acromegalic **patient** receives an adequate **calcium** intake and sex **hormone replacement therapy.**

```
=> d his ful

     FILE 'REGISTRY' ENTERED AT 10:36:17 ON 03 DEC 2004
                E HPTH/CN
L1            1 SEA ABB=ON  "HPTH-(1-34)"/CN
                E VITAMIN D/CN
L2            1 SEA ABB=ON  "VITAMIN D"/CN
                E CA
                E CA/CN
                E CALCIUM/CN
L3            1 SEA ABB=ON  CALCIUM/CN

     FILE 'HCAPLUS' ENTERED AT 10:37:08 ON 03 DEC 2004
L4       161514 SEA ABB=ON  (?BONE?(3A)(?FRACT? OR ?FORM? OR ?LOSS? OR ?LOSE?)
                OR ?OSTEPOROSIS? OR ?OSTEOGENESIS? OR ?SPINE? OR ?SPINAL?)
L5         1004 SEA ABB=ON  L4 AND (L1 OR HPTH(W)(1-34) OR ?HPTH? OR ?HUMAN?(W)
                ?PARATHYROID?(W)?HORMONE?(3W)(1-34) OR ?HORMONE?(W)?REPLACEMENT
                ?(W)?THERAPY?)
L6          300 SEA ABB=ON  L5 AND (L2 OR L3 OR ?VITAMIN?(W)D OR CA OR
                ?CALCIUM?)
L7          229 SEA ABB=ON  L6 AND (AGE? OR ?AGING? OR ?GERIAT? OR ?SENIL? OR
                ?MENOPAUS? OR ?KLINEFELTER?(W)?SYNDROM? OR ?HYPOGONAD? OR
                ?GONAD?(W)?DISORDER?)
L8          168 SEA ABB=ON  L7 AND (?HUMAN? OR ?PATIENT?)
L9            2 SEA ABB=ON  L8 AND (?REDUCE? OR ?LESSEN? OR ?CONTROL? OR
                ?DECREAS?)(W)?RISK?
L10       * 168 SEA ABB=ON  L8 OR L9
L11          28 SEA ABB=ON  L10 AND (?METHOD? OR ?TECHNIQ?)

     FILE 'MEDLINE, BIOSIS, EMBASE, JAPIO, JICST-EPLUS' ENTERED AT 10:46:58 ON
     03 DEC 2004
L12         343 SEA ABB=ON  L11
L13         241 DUP REMOV L12 (102 DUPLICATES REMOVED)
L14          67 SEA ABB=ON  L13 AND (MONITOR? OR DETECT? OR DETERMIN?)
L15           1 SEA ABB=ON  L14 AND HPTH(W)(1-34)
L16           1 SEA ABB=ON  L14 AND ?HUMAN?(W) ?PARATHYROID?(W) ?HORMON?(W)(1-3
                4)
L17           1 SEA ABB=ON  L15 OR L16
L18           7 SEA ABB=ON  L14 AND ?GONAD?
L19           8 SEA ABB=ON  L17 OR L18
L20          57 SEA ABB=ON  L14 AND (AGE? OR AGING? OR GERIAT? OR SENIL?)
L21        * 57 SEA ABB=ON  L19 OR L20
```

* saved, should you want to [illegible]